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Toxo XV: A Congress at the Birthplace of Toxoplasma.

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TrendsTalk

Toxo XV: A Congress at the Birthplace of *Toxoplasma*

In this TrendsTalk article, the organizers of the 15th International Congress on *Toxoplasma* Biology and Toxoplasmosis, Professors Jorge Gomez Marin and Alejandra de la Torre, bring the highlights of this event and the key outcome from the inaugural workshop on the environmental transmission of *Toxoplasma gondii* organized by Doctors Aurélien Dumètre and Karen Shapiro. 15th International *Toxoplasma* congress group photo.

Professor Jorge Gomez Marin

President of *Toxo XV*, leads the Group of Molecular Parasitology (GEPAMOL) at the Universidad del Quindío in Colombia. His group contributed greatly to the understanding of the epidemiology, risk factors, and role of virulence factors in clinical toxoplasmosis.

How was the experience organizing *Toxo XV* in Colombia? How will this congress impact researchers in Colombia and Latin America?

The first International *Toxoplasma* Congress was held in 1989 in Squam Lake, New Hampshire. After 30 years, the research community decided that it was time for the congress to be celebrated outside North America and Europe. Previously, many lines of evidence suggested that *T. gondii* originated as a species in South America. In 2017, Dr Daniel Ajzenberg's group, by using a geostatistical approach and testing a large number of hypothetical origins across the world, identified South America, and more specifically Colombia, as the most likely origin of the parasite. Thus, it was a special place to celebrate this congress. For many young researchers from Colombia and other Latin American countries, it was the first and a unique opportunity to participate in a top scientific event with an impact that will last for many years and become paramount for these new generations of parasitologists.

What were the new discoveries on biology and host-parasite interactions of *Toxoplasma* that marked this congress this year?

Undoubtedly the single cell transcriptome screening was the star at this event. This screening method started from CRISPR arrayed libraries and showed its power and potential to identify new *T. gondii* transcriptional effectors. This technique

was key for the identification of the genes responsible for bradyzoite differentiation. Another focus of interest for the *T. gondii* research community is the human guanylate binding proteins (GBPs) that were at the center of the immunological studies for many groups. It is fascinating to see how it has advanced our understanding of the interferon-mediated effector mechanisms. These mechanisms are determinant to understand how *T. gondii* virulence factors influence the human immune system.

What is the 'state of the art' of genomic studies in *Toxoplasma* infection?

ToxoDB (https://toxodb.org) has evolved greatly and many functionalities have been incorporated recently, making it a powerful tool for the *T. gondii* research community. It is possible to analyze complete genomes of strains, metabolic pathways, expression profiles, and much more. Its possibilities are near infinite given the amount of data that is freely available. I consider that all members of the *T. gondii* research community should be responsible for supporting the preservation of this tool. We need to create an international consortium for the continuing construction of this essential genomic database. Regarding *T. gondii* mitochondrial DNA, this remains elusive to a complete analysis, and further research is still much needed. *T. gondii* mitochondria are nearly impossible to purify but can be enriched. Jessica Kissinger's laboratory at the University of Georgia found that the order of the mtDNA units is not conserved and that it is composed of 21 sequence blocks.

Professor Alejandra de-la-Torre
Member of the *Toxo XV* scientific organizing committee, is an expert ophthalmologist in uveitis and leads clinical and basic research in toxoplasmosis at the Universidad del Rosario in Bogota, Colombia.

Are there advances of the basic biology research on *Toxoplasma* that can impact clinical management or vaccine development?

The years to come are exciting in relation to the possibilities for new and better vaccine candidates, given our better understanding of the immune response and the chemical details for antigen recognition by lymphocytes, as shown by Dr Manuel Elkin Patarroyo in his inaugural keynote talk. This new knowledge is giving us essential clues to select protective peptides. It is also noteworthy that the explosion of new compounds that act as inhibitors of invasion and specific metabolic pathways is based on combined biochemistry and genomic screening strategies, showing the importance of the interdisciplinary work between chemists and molecular biologists. Regarding the relationship between chronic toxoplasmosis and mental diseases, although many researchers remains skeptical about a causal association, it is interesting to see how *Toxoplasma* can indeed induce inflammatory local responses but with individual variability, explaining why only a subset of infected individuals have *Toxoplasma*-related behavioral changes. Also fascinating was the development of intravital imaging techniques that revealed the detection of motile, infected cells trafficking the parasites in the central nervous system.

What were the aims of the inaugural meeting of the Environmental *Toxoplasma* Transmission workshop?

Oocysts are the least studied stage of the parasite, but are critically important for driving the epidemiology of toxoplasmosis in animals and humans. Formal opportunities for bringing together research teams focused on *T. gondii* oocyst studies and environmental transmission have been limited. To initiate a solution, the objectives of this workshop were to bring together international researchers investigating oocyst biology and *T. gondii* environmental transmission. Experts in the field were

Dr Karen Shapiro
Associate professor at the University of California Davis, School of Veterinary Medicine. She has made important contributions to our understanding of *Toxoplasma* transmission in the environment and oocyst transport from land to sea with implications for marine mammal health.

invited to discuss past and current knowledge on oocyst biology, transmission, and epidemiology of *T. gondii* in tropical to arctic regions. A field expedition to the Bremen La Popa Natural Reserve was also included in the second day of the workshop. This habitat can support the sylvatic *T. gondii* life cycle among wild cats and their prey, with potential for oocyst contamination within the drinking water catchment area for the municipality of Armenia. Deforestation of the region and increased agricultural land use have further facilitated the contact among domestic cats, wild felids, humans, and other intermediate hosts, resulting in increased opportunities for exchange of *T. gondii* strains between wild and anthropogenic environments and the emergence of new virulent genotypes.

Can you tell us what were the proposed research priorities from the round table discussion of the experts?

In the round table discussions, high-priority topics were proposed for future research endeavors to address missing links in the biology and epidemiology of *T. gondii* oocyst transmission:

- The molecular basis for oocyst persistence in the environment is still unknown. Development of new *in vitro/in vivo* oocyst production systems should help further investigations to decipher oocyst biology at the molecular level.
- Current data on oocyst shedding has been published almost exclusively for experimentally infected cats. Field investigations are warranted for evaluating duration, recurrence, load, and genotypes of oocysts shed by naturally exposed pet cats, feral cats, and wild felids. Habitat change can also impact domestic and wild felid biology and behavior. Deforestation and human poaching can reduce preferred prey species of wild felids, forcing them to shift prey types or consume smaller prey more often. Such niche-shifting behavior may alter the frequency of exposure to *T. gondii*-infected prey, as well as the parasite genotypes ingested by felids, which may result in the creation of new genotypes via sexual recombination in their intestinal epithelium.
- Climate variability may impact the persistence, transport, and fate of viable oocysts in the environment. Physicians from regions with a high burden of human toxoplasmosis have noted a rise in clinical cases (e.g., ocular toxoplasmosis) following heavy rainfall events. Studies are needed to evaluate how shifting temperature, precipitation, and humidity patterns can affect the contamination of water and foods with infective oocysts and drive the onset of acute disease. Characterization of *T. gondii* strains should be pursued from more wild species, including felids in tropical areas, following a gradient from anthropized to wild biotopes to evaluate genetic diversity among strains and their association with parasite virulence. This would require standardization and refinement of genotyping methods.
- Information regarding the spatiotemporal contamination of water sources for drinking and crop irrigation is lacking in many regions. Methods for oocyst detection in water and other environmental matrices require standardization among laboratories and countries – with options for low- and high-income approaches depending on available resources
- As reducing the load of oocysts in the environment is logistically difficult, there is an urgent need for effective, affordable, and practical water-treatment strategies, especially in lower-income countries. Chlorine-based products, UV, or ozone used as the single disinfection treatment are limited in effectiveness. Implementation of filtration systems and distribution network maintenance could help to reduce *T. gondii* contamination at the faucet.

Dr Aurélien Dumètre
Associate professor in the Laboratory of Tropical and Mediterranean Infections at Aix-Marseille University in France. He is an internationally recognized researcher for the development of new tools to study the properties and detection of *T. gondii* oocysts in the environment.

As lead of the inaugural workshop on Environmental *Toxoplasma* Transmission, can you tell us what were the recommendations for future work?

The workshop was a very productive meeting and an opportunity for face-to-face dialogue and discussion among the top researchers in the field. A general consensus among the workshop participants is that establishing a formal platform for continuous exchange of knowledge and training in the field of environmental *T. gondii* transmission is essential for mitigating illness in people and animals.
Several specific recommendations were made, including:

- Creating a network of scientists invested in research targeting oocyst biology and environmental transmission of *T. gondii* among groups across international borders and multigeographical regions.
- Facilitating student/researcher exchange and providing practical training for stakeholders and scientists on oocyst detection methods in diverse matrices as well as epidemiological approaches targeting *T. gondii* transmission from molecular to ecosystem scales.
- Establishing a biannual meeting or workshop to facilitate in-person dialogue and share recent research findings; these meetings will encourage the attendance of students, postdoctoral and professional researchers, relevant stakeholders, and educators.

Who participated in making this first-ever workshop on environmental toxoplasmosis happen?

This workshop was made possible through contributions of experts and enlightening round table discussions held by the workshop speakers and participants, including Drs Lilian Bahia-Oliveira, Jon Boyle, Patricia Conrad, David Ferguson, Pia K. Muchaal, Frank Seeber, Elizabeth VanWormer, and Isabelle Villena. We also extend our gratitude to Dr Hugo Mantilla Meluk for guiding the field expedition and sharing his expertise, as well as biologists and reserve managers at the Bremen La Popa Natural Reserve in Filandia-Quindio, Colombia. The workshop was funded by 'Vicerrectoria de Investigaciones' of the Universidad del Quindio.

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